PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 37003-304483	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US03/19652	International filing date *(day/month/year)* 23 June 2003 (23.06.2003)	Priority date *(day/month/year)* 21 June 2002 (21.06.2002)
International Patent Classification (IPC) or national classification and IPC IPC(7): C07K 16/00; A61K 39/395 and US Cl.: 530/387.1, 387.3, 388.1; 424/130.1, 133.1, 181.1, 183.1		
Applicant IDEC PHARMACEUTICALS CORP.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of ___ sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☒ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
14 January 2004 (14.01.2004)	01 December 2004 (01.12.2004)
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer David J Blanchard Telephone No. (571) 272-0827 DEBORAH A. THOMAS PARALEGAL SPECIALIST ~~GROUP 1800~~

Form PCT/IPEA/409 (cover sheet)(July 1998)

INTERNATIONAL PRELIMIN[redacted] EXAMINATION REPORT

International application No.
PCT/US03/19[redacted]

I. Basis of the report

1. With regard to the elements of the international application:*

☒ the international application as originally filed.

☒ the description:
pages 1-24 as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the claims:
pages 25-38, as originally filed
pages NONE, as amended (together with any statement) under Article 19
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☒ the drawings:
pages 1-7, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

☐ the sequence listing part of the description:
pages NONE, as originally filed
pages NONE, filed with the demand
pages NONE, filed with the letter of _____.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

☐ the language of a translation furnished for the purposes of international search (under Rule23.1(b)).

☐ the language of publication of the international application (under Rule 48.3(b)).

☐ the language of the translation furnished for the purposes of international preliminary examination(under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

☐ contained in the international application in printed form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages NONE

☐ the claims, Nos. NONE

☐ the drawings, sheets/~~fig~~ NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).*
*** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.*

INTERNATIONAL PRELIMIN[redacted] EXAMINATION REPORT

International application No.
PCT/US03/19[redacted]

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Inventive Step (IS)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO
Industrial Applicability (IA)	Claims	Please See Continuation Sheet	YES
	Claims	Please See Continuation Sheet	NO

2. CITATIONS AND EXPLANATIONS
Please See Continuation Sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

Application No Patent No.	Publication Date *(day/month/year)*	Filing Date *(day/month/year)*	Priority date (valid claim) *(day/month/year)*
US 2003/0113316 A1	19 June 2003 (19.06.2003)	25 July 2002 (25.07.2002)	25 July 2001 (25.07.2001)
US 2003/0138417 A1	24 July 2003 (24.07.2003)	08 November 2002 (08.11.2002)	08 November 2001 (08.11.2001)

2. Non-written disclosures (Rule 70.9)

Kind of non-written disclosure	Date of non-written disclosure *(day/month/year)*	Date of written disclosure referring to non-written disclosure *(day/month/year)*

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

V.1. Reasoned Statements:
The opinion as to Novelty was positive (Yes)with respect to claims 13, 15-17, 19, 33, 35-39, 53, 55-59, 73, 75-79, 94-98, 102-121
The opinion as to Novelty was negative (No) with respect to claims 1-12, 14, 18-19, 32, 34, 40-52, 54, 60-72, 74, 80-93, 99-101
The opinion as to Inventive Step was positive (Yes)with respect to claims NONE
The opinion as to Inventive Step was negative(NO) with respect to claims 1-121
The opinion as to Industrial Applicability was positive (YES) with respect to claims 1-121
The opinion as to Industrial Applicability was negative(NO) with respect to claims NONE

Claims 1-12, 14 and 18-19 lack novelty under PCT Article 33(2) as being anticipated by Kakuta et al.

Claims 1-12, 14 and 18-19 are drawn to antibody compositions consisting essentially of histidine or acetate buffer at concentration ranges of 2mM to about 48mM; 3mM to about 48mM, 4mM to about 45mM; 5mM to about 40mM; 20mM to about 25mM and the pH is in the range from about 4-7.5; 4.5-7; 5-6.5; 5.5-6 and the antibodies are chimeric or humanized and the concentration of the antibodies is at least 50 mg/mL and at least 100 mg/mL.

Kakuta et al teach antibody compositons in histidine buffer having various concentration ranges that overlap or touch the claimed buffer concentration ranges (e.g., see pages 4-6 and example 6) as well as the claimed pH ranges and the antibodies are chimeric or humanized (see pages 7-8) and the antibodies are preferably at least 100 mg/mL (see page 13). The teachings of Kakuta et al are sufficiently specific that the skilled artisan would readily envisage the instantly claimed buffer concentrations, pH values, and antibody concentrations from the teachings of Kakuta et al.

Claims 1-12, 14, 18, 20-32, 34, 40-52, 54, 60-72, 74, 80-93 and 99-101 lack novelty under PCT Article 33(2) as being anticipated by Lam et al

The claims have been described supra. Claims 20-32, 34, 40-52, 54, 60-72, 74, 80-93 and 99-101 are drawn to the antibody compositions that comprise antibodies that binds specific antigens (i.e., CD4, CD20) and a method for producing a concentrated antibody compositions by subjecting the initial antibody preparation to membrane filtration, wherein the antibody compositions are in histidine or acetate buffers having the previously said concentration ranges and pH ranges. The concentrated antibody compositions may further comprise one or more pharmaceutically acceptable carriers to produce a pharmaceutical composition. The claims also encompass an improved method of therapy that includes administration of said pharmaceutical composition comprising said antibody compositions for treating a patient having cancer, allergic disorders, autoimmune diseases or lymphoma.

Lam et al teach antibody compositions and pharmaceutical compositions comprising monoclonal antibodies, chimeric or humanized antibodies in histidine or acetate buffers having a pH in the pH range from about 4.5-about 6.0, most preferably of about pH 5.0 and the pharmaceutical compositions comprise one or more pharmaceutically acceptable carriers, excipients or stabilizers (see entire document especially bridging paragraph of columns 22-23, columns 5-9 and 22-23 and Tables 1, 15 and 16). Lam et al teach an antibody composition comprising an anti-CD20 antibody in 25mM histidine at pH5, 6.5 or 7.5 (see Figure 24 and legend at column 4). Applicant is reminded that when by a recitation of ranges or otherwise, a claim covers several compositions, the claim is anticipated if one of them is in the prior art. See MPEP 2131.03. Lam et al teach antibody concentration using a protein concentration filter/ultrafiltration unit (see column 21, lines 33-37). Lam et al teach a method of therapy comprising administering said pharmaceutical compositions to a patient (preferably human; column 23, line 33) for treating disorders including rheumatoid arthritis (see column 24) (see columns 23-24).

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Claims 1-121 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

----------NEW CITATIONS----------

US 6,171,586 B1 (LAM et al) 9 January 2001, see entire document, especially bridging paragraph of columns 6-7, columns 7-10, 21-24, Table 1 and examples.